

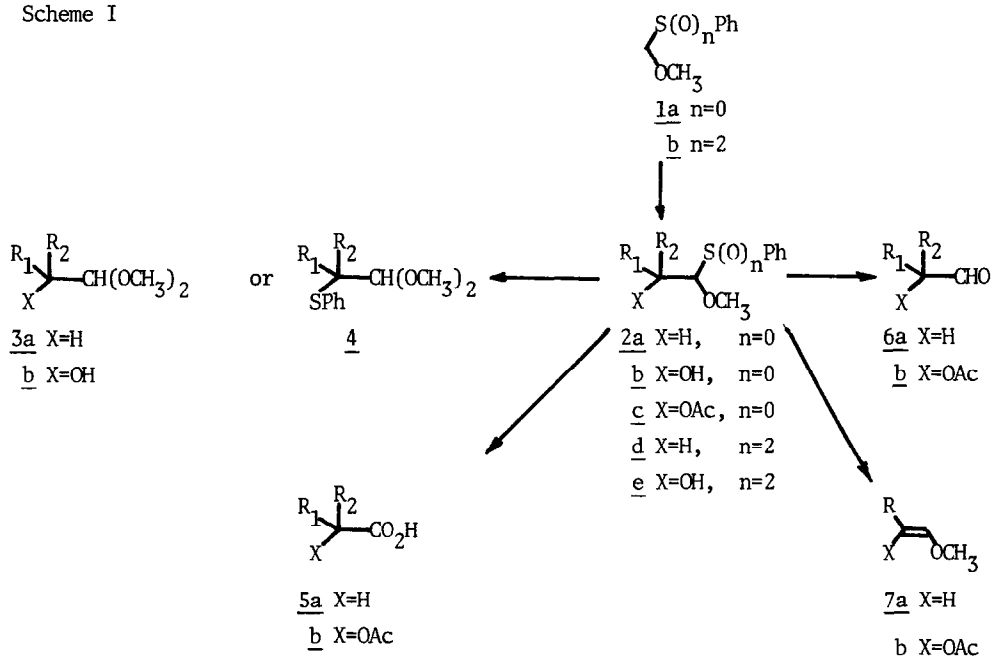
SYNTHETIC APPLICATION OF PHENYLTHIO- AND PHENYLSULFONYLMETHYL ETHERS
 TO ALDEHYDES, METHYLALS, CARBOXYLIC ACIDS, AND ENOL OR DIENOL ETHERS

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Summary: Novel synthetic application of the title compounds to aldehydes, methylals, carboxylic acids, and enol or dienol ethers has been newly developed.

Carbon-carbon bond formation involving carbon homologation is one of the more important problems in synthetic organic chemistry. Above all, development of effective reagents for one carbon elongation has been the subject of extensive interest. In line with this, sulfur derivatives such as S,S-acetals (1,3-dithianes) and their S-oxides (FAMSO) have received considerable attention for these two decades.¹⁾ However, these reagents are not always employable because metallic salts or acidic conditions are generally required for their conversion into carbonyl compounds. In our program for developing more versatile reagents, we found that methoxy(phenylthio)methane (1a) and methoxy(phenylsulfonyl)methane (1b) can serve as useful reagents for one carbon homologation. To our knowledge, synthetic application of these compounds has been rather limited.²⁻⁴⁾ Herein we wish to report a much more versatile and novel synthetic application of 1 which gives rise to a variety of compounds as depicted in Scheme I.

Scheme I



Notable features of these reagents are as follows; i) a general synthetic method for methylals is provided, ii) synthetically useful carboxylic acids can be obtained by a simple procedure, iii) conversion to aldehydes proceeds under almost neutral conditions, and iv) there have opened new routes for enol or dienol ethers which are difficult to obtain by other methods. It should be noted that 1a and 1b usually possess their own utilities, but in some cases, they are complementary to each other.

Carbon-carbon bond formation was easily achieved by treating anions of 1⁵⁾ with organic halides or carbonyl compounds in THF at -78 °C. Trost *et al.* reported that the β -hydroxy compounds obtained from 1a and lactones can be converted to the corresponding methylals by use of mercuric chloride-*red* mercuric oxide or iodine in methanol.²⁾ As shown in Table 1, we found that conversion of the alkylation products of 1a to the corresponding methylals 3 is effected by a catalytic amount of *p*-toluenesulfonic acid in refluxing methanol for 2 h. Unfortunately, however, this method was found not to be effective for β -hydroxy derivatives 2b which resulted in unsatisfactory conversions even after a prolonged reaction time (entry 4 and 5) or afforded α -phenylthiomethylals 4 exclusively (entry 6, 7, and 8). By contrast, it was revealed that employment of the sulfonyl derivatives 2d and 2e induced no rearrangement of the phenylsulfonyl group to give corresponding methylals 3 in high yields irrespective of starting material. Thus, the sulfonyl compounds seem to serve as versatile synthons for methylals.

Table 1. Conversion of 2 into methylals 3 or 4.

entry	<u>2</u>				yield, % ^a	
	R ₁	R ₂	X	n	<u>3</u>	<u>4</u>
1	C ₁₃ H ₂₇	H	H	0	78	
2	Ph	H	H	0	72	
3	C ₁₀ H ₁₇ CH(OH)	H	H	0	70	
4	C ₅ H ₁₁	H	OH	0	21	
5	(CH ₂) ₅		OH	0	30	
6	Ph	H	OH	0		80
7	CH ₃	CH ₃	OH	0		58
8	Ph	CH ₃	OH	0		56
9	C ₁₃ H ₂₇	H	H	2	92	
10	Ph	H	H	2	99	
11	C ₅ H ₁₁	H	OH	2	91	
12	(CH ₂) ₅		OH	2	90	

a) Isolated yields after column chromatography.

Further, phenylthio derivatives 2a and 2c can be directly converted into carboxylic acids 5a and 5b, respectively (see Table 2) by Jones type oxidation (CrO₃-H₂SO₄ at 0 °C for 1 h in acetone). It is possible that the reaction proceeds *via* an aldehyde intermediate from an initially formed labile sulfoxide since more than 2 equiv of the oxidizing reagent is required. It is noteworthy

Table 2. Conversion of 2a and 2c to carboxylic acids 5.

entry	<u>2a</u> and <u>2c</u>	<u>5</u> yield, % ^a
1		78
2		70
3		55
4		60
5		52

a) Isolated yields after column chromatography.

that synthetically useful α -acetoxycarboxylic acids can be obtained in good yields by this method and that allylic derivatives are not isomerized into conjugation.

In the course of the study on oxidation of 2a and 2c, we found quite surprisingly that aldehydes 6 were produced in good yields. Treatment of 2a and 2c with m-CPBA at $-5 - 0$ °C in toluene yielded the corresponding sulfoxides, which are stable below 0 °C, but decompose between 10 - 40 °C to give aldehydes 6a and 6b, respectively. On the other hand, rapid heating of the sulfoxides formed *in situ* to 120 °C provided enol or dienol ethers 7. The results are summarized

Table 3. Conversion of 2a and 2c to aldehydes 6 or enol (dienol) ethers 7.

entry	<u>2a</u> and <u>2c</u>	<u>6</u>	Yield, % ^a	<u>7</u>	E/Z yield, % ^a
1			78		60/40 85
2			88		60/40 80
3			74		55/45 72
4			30 ^b		53/47 68
5			40		64/36 70
6			44		75/25 72

a) Isolated yields after column chromatography unless otherwise noted.

b) Determined by the ¹H NMR spectrum of crude products which are contaminated by the corresponding dienol ether (50% yield). Purification by column chromatography resulted in decomposition of the aldehyde.

in Table 3. The notable features of this method are twofold; i) aldehydes or enol ethers can be obtained from common precursors only by changing the reaction temperature, and ii) the reaction proceeds under almost neutral conditions, so that coexisting acid-sensitive functional groups such as tetrahydropyranyl ethers and acetals are not affected by the reaction conditions.

Finally, we found that enol or dienol ethers can also be prepared from the corresponding sulfonyl derivatives 2d (see Table 4). Desulfonylation occurred easily by treating these compounds with *t*-BuOK in THF.⁶⁾ When homoallylic phenylsulfonyl derivatives were employed, dienol ethers which are useful for the regioselective Diels-Alder reaction⁷⁾ were formed with a high degree of stereoselectivity for the E isomer. This is quite important since the Z isomer is inert to the Diels-Alder reaction.

Table 4. Conversion of 2d to enol (dienol) ethers 7.

entry	<u>2d</u>	reaction temp °C	<u>7</u>	E/Z	yield, % ^a
1		66		30/70	72
2		20		99/1	68
3		20		82/18	76
4		20		93/7	57

a) Isolated yields after column chromatography.

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References and Note

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